FIG. 1

```
                    ccggaattcccgggtcgacccacgcgtccggcccccattcaagaagccgctcagctatcccggccagcacagggcgc
                    ccggcgcgcctcggagcgcaagttcctcgccttctcctgcccgctcgctgggcattatgcggccaagcagccgagccccagtcctc
        5           ctcctcctcctgctcctccggctcctcctgcggcccgagcggctcagctctcggcaggcggcggcgttgctcagccgagcgcagac
                    gggaccctcgcagcgagacctcagcgactcctaaagtcaaaagttggcggcgggcgccgggctccgcgcgctctccacggccgctg
                    cctcgcgtcgccgccgcagccaaggagggcaggagggagggggtgggggcagcggaggagggggtgggaagcaccatgcagtttg
                    tatcctgggccacactgctaacgctcctggtgcgggacctggccgagatggggagcccagacgccgcggcggccgtgcgcaaggac
                    aggctgcacccgagcaagtgaaattattagagaccctgagcgaatacgaaatcgtgtctcccatccgagtgaacgctctcggaga
        10          acccttcccacgaacgtccacttcaaaagaacgcgacggagcattaactctgccactgacccctggcctgccttcgcctcctcct
                    cttcctcctctacctcctcccaggcgcattaccgcctctctgccttcggcagcagtttctatttaatctcaccgccaatgccgga
                    tttatcgctccactgttcactgtcaccctcctcgggacgcccggggtgaatcagaccaagtttattccgaagaggaagcggaact
                    caagcactgtttctacaaaggctatgtcaataccaactccgagcacacggccgtcatcagcctctgctcaggaatgctgggcacat
                    tccggtctcatgatggggattatttttattgaaccactacagtctatggatgaacaagaagatgaagaggaacaaaacaaaccccac
        15          atcatttataggcgcagcgcccccagagagagccctcaacaggaaggcatgcatgtgacacctcagaacacaaaaataggcacag
                    taaagacaagaagaaaaccagagcaagaaaatgggagaaaggattaacctggctggtgacgtagcagcattaaacagcggcttag
                    caacagaggcattttctgcttatggtaataagacgacaacacaagagaaagaggacccacagaaggacaaaacgttttttatcc
                    tatccacggtttgtagaagtcttggtggtggcagacaacagaatggtttcataccatggagaaaaccttcaacactatattttaac
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        20          ataatgaacaggatgggccttccatatcttttaatgctcagacaacattaaaaaacttttgccagtggcagcattcgaagaacagt
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                    ggctgaactgggaaccatttgtgatccctatagaagctgttctattagtgaagatagtggattgagtacagcttttacgatcgccc
                    atgagctgggccatgtgtttaacatgcctcatgatgacaacaacaaatgtaaagaagaaggagttaagagtccccagcatgtcatg
                    gctccaacactgaacttctacaccaacccctggatgtggtcaaagtgtagtcgaaaatatatcactgagttttttagacactggtta
        25          tggcgagtgtttgcttaacgaacctgaatccagaccctacccttgcctgtccaactgccaggcatcctttacaacgtgaataaac
                    aatgtgaattgattttttggaccaggttctcaggtgtgcccatatatgatgcagtgcagacggctctggtgcaataacgtcaatgga
                    gtacacaaaggctgccggactcagcacacaccctgggccgatgggacggagtgcgagcctggaaagcactgcaagtatggattttg
                    tgttcccaaagaaatggatgtccccgtgacagatggatcctggggaagttggagtcccctttggaacctgctccagaacatgtggag
                    ggggcatcaaaacagccattcgagagtgcaacagaccagaaccaaaaaatggtggaaaatactgtgtaggacgtagaatgaaattt
        30          aagtcctgcaacacggagccatgtctcaagcagaagcgagacttccgagatgaacagtgtgctcactttgacgggaagcattttaa
                    catcaacggtctgcttcccaatgtgcgctgggtccctaaatacagtggaattctgatgaaggaccggtgcaagttgttctgcagag
                    tggcagggaacacagcctactatcagcttcgagacagagtgatagatggaactccttgtggccaggacacaaatgatatctgtgtc
                    cagggcctttgccggcaagctggatgcgatcatgtttttaaactcaaaagcccggagagataaatgtggggtttgtggtggcgataa
                    ttcttcatgcaaaacagtggcaggaacatttaatacagtacattatggttacaatactgtggtccgaattccagctggtgctacca
        35          atattgatgtgcggcagcacagtttctcaggggaaacagacgatgacaactacttagctttatcaagcagtaaaggtgaattcttg
                    ctaaatggaaactttgttgtcacaatggccaaaagggaaattcgcattgggaatgctgtggtagagtacagtgggtccgagactgc
                    cgtagaaagaattaactcaacagatcgcattgagcaagaacttttgcttcaggttttgtcggtgggaaagttgtacaaccccgatg
                    tacgctattcttttcaatattccaattgaagataaacctcagcagttttactggaacagtcatgggccatggcaagcatgcagtaaa
                    ccctgccaaggggaacggaaacgaaaacttgtttgcaccagggaatctgatcagcttactgtttctgatcaaagatgcgatcggct
        40          gccccagcctggacacattactgaaccctgtggtacagactgtgacctgaggtggcatgttgccagcaggagtgaatgtagtgccc
                    agtgtggcttgggttaccgcacattggacatctactgtgccaaatatagcaggctggatgggaagactgagaaggttgatgatggt
                    ttttgcagcagccatcccaaaccaagcaaccgtgaaaaatgctcagggaatgtaacacgggtggctggcgctattctgcctggac
                    tgaatgttcaaaaagctgtgacggtgggacccagaggagaagggctatttgtgtcaatacccgaaatgatgtactggatgacagca
                    aatgcacacatcaagagaaagttaccattcagaggtgcagtgagttcccttgtccacagtggaaatctggagactggtcagagtgc
        45          ttggtcacctgtggaaaagggcataagcaccgccaggtctggtgtcagtttggtgaagatcgattaaatgatagaatgtgtgaccc
```

tgagaccaagccaacatctatgcagacttgtcagcagccggaatgtgcatcctggcaggcgggtccctggggacagtgcagtgtca

cttgtggacagggataccagctaagagcagtgaaatgcatcattgggacttatatgtcagtggtagatgacaatgactgtaatgca

gcaactagaccaactgatacccaggactgtgaattaccatcatgtcatcctcccccagctgccccggaaacgaggagaagcacata

cagtgcaccaagaacccagtggcgatttgggtcttggaccccatgctcagccacttgtgggaaaggtacccggatgagatacgtca

gctgccgagatgagaatggctctgtggctgacgagagtgcctgtgctaccctgcctagaccagtggcaaaggaagaatgttctgtg

acaccctgtgggcaatggaaggccttggactggagctcttgctctgtgacctgtgggcaaggtagggcaacccggcaagtgatgtg

tgtcaactacagtgaccacgtgatcgatcggagtgagtgtgaccaggattatatcccagaaactgaccaggactgttccatgtcac

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tgttgttgtatgtcaggatgaaaatggatacaccgcaaacgactgtgtggagagaataaaaacctgatgagcaaagagcctgtgaat

ccggcccttgtcctcagtgggcttatggcaactggggagagtgcactaagctgtgtggtggaggcataagaacaagactggtggtc

tgtcagcggtccaacggtgaacggtttccagatttgagctgtgaaattcttgataaacctcccgatcgtgagcagtgtaacacaca

tgcttgtccacacgacgctgcatggagtactggcccttggagctcgtgttctgtctcttgtggtcgagggcataaacaacgaaatg

tttactgcatggcaaaagatggaagccatttagaaagtgattactgtaagcacctggctaagccacatgggcacagaaagtgccga

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ctgtcagatcggaacacacaaaatagccagagagaccgagtgcaacccatacaccagaccggagtcggaacgcgactgccaaggcc

cacggtgtcccctctacacttggagggcagaggaatggcaagaatgcaccaagacctgcggcgaaggctccaggtaccgcaaggtg

gtgtgtgtggatgacaacaaaaacgaggtgcatggggcacgctgtgacgtgagcaagcggccggtggaccgtgaaagctgtagttt

gcaaccctgcgagtatgtctggatcacaggagaatggtcagaggtaccgtcctgggaactgtaaccatcgtcagctcagccatggc

ctgagagtggcagagggatgagtggagggatgagtgcaggaatgtgggagacttgaggctacccgcccgatttgccactgtgaact

gtgtgtttttctgacaagtcctcagctttcccaagctagaattccttgtatgcaaagcgggagagatgtaagagatggtctctaagt

cccttcaggtctacattctgtgattcaccttgatgtcctattggcataaagaagaaattattacaggggctgcaaactcataggat

gctgtgaggtgcctgaagacagttaagtataagaaaatattgtagtgccagggatacaacaaggagagatggcaactgtgacaaac

tagcacatgctgtgtgaagggagcagaatctctttcactccagctgtggccatgcagaaatgtggtctagcgttaccagacctgat

ttttcaagagaggctaaaaatctggactagtatgtgagatttcctaacttgaaaatgggggctgaaatttttggttttaaaacatt

gtaaggggcaaacaaaccccttttcatgaaccagatgtgttgtgcctgtttaacaaacagcttcagaggaagaaaataattttctat

aatatccgaagtatctcaagtac

FIG. 2

```
          mqfvswatlltllvrdlaemgspdaaaavrkdrlhprqvklletlseyeivspirvnalgepfptnvhfkrtrrsins
  5    atdpwpafassssssstssqahyrlsafgqqflfnltanagfiaplftvtllgtpgvnqtkfyseeeaelkhcfykgyvntnsehta
       vislcsgmlgtfrshdgdyfieplqsmdeqedeeeqnkphiiyrrsapqrepstgrhacdtsehknrhskdkkktrarkwgerinl
       agdvaalnsglateafsaygnktdntrekrthrrtkrflsyprfvevlvvadnrmvsyhgenlqhyiltlmsivasiykdpsignl
       inivivnlivihneqdgpsisfnaqttlknfcqwqhsknspggihhdtavlltrqdicrahdkcdtlglaelgticdpyrscsise
       dsglstaftiahelghvfnmphddnnkckeegvkspqhvmaptlnfytnpwmwskcsrkyitefldtgygeclinepesrpyplpv
  10    qlpgilynvnkqcelifgpgsqvcpymmqcrrlwcnnvngvhkgcrtqhtpwadgtecepgkhckygfcvpkemdvpvtdgswgsw
       spfgtcsrtcgggiktairecnrpepknggkycvgrrmkfkscntepclkqkrdfrdeqcahfdgkhfningllpnvrwvpkysgi
       lmkdrcklfcrvagntayyqlrdrvidgtpcgqdtndicvqglcrqagcdhvlnskarrdkcgvcggdnsscktvagtfntvhygy
       ntvvripagatnidvrqhsfsgetdddnylalsssskgefllngnfvvtmakreirignavveysgsetaverinstdrieqelllq
       vlsvgklynpdvrysfnipiedkpqqfywnshgpwqacskpcqgerkrklvctresdqltvsdqrcdrlpqpghitepcgtdcdlr
  15    whvasrsecsaqcglgyrtldiycakysrldgktekvddgfcsshpkpsnrekcsgecntggwrysawtecskscdggtqrrraic
       vntrndvlddskcthqekvtiqrcsefpcpqwksgdwseclvtcgkghkhrqvwcqfgedrlndrmcdpetkptsmqtcqqpecas
       wqagpwgqcsvtcgqgyqlravkciigtymsvvddndcnaatrptdtqdcelpschpppaapetrrstysaprtqwrfgswtpcsa
       tcgkgtrmryvscrdengsvadesacatlprpvakeecsvtpcgqwkaldwsscsvtcgqgratrqvmcvnysdhvidrsecdqdy
       ipetdqdcsmspcpqrtpdsglaqhpfqnedyrprsaspsrthvlggnqwrtgpwgacsstcaggsqrrvvvcqdengytandcve
  20    rikpdeqracesgpcpqwaygnwgectklcgggirtrlvvcqrsngerfpdlsceildkppdreqcnthacphdaawstgpwsscs
       vscgrghkqrnvycmakdgshlesdyckhlakphghrkcrggrcpkwagawsqcsvscgrgvqqrhvgcqigthkiaretecnpy
       trpeserdcqgprcplytwraeewqectktcgegsryrkvvcvddnknevhgarcdvskrpvdrescslqpceyvwitgewsevps
       wel*
```

25

Fig. 3

Domain structure of ADAMTS-SI

Signal peptide (1-18), Prodomain (19-287), Furin cleavage site (288),
Metalloproteinase domain (289-478), Zinc binding motif (434-446),
Heparin binding motif (478-482), Disintegrin domain (509-578),
Thrombospondin motif (589-642), Spacer region (643-1014),
Thrombospondin submotifs (1001-1053, 1056-1108, 1111-1165, 1186-1239,
1240-1295, 1332-1383, 1386-1439,1445-1500, 1501-1554, 1559-1612)

ADAMTS-SI
1630 aa

β

1   CCGGAATTCC CGGGTCGACC CACGCGTCCG GCCCCCCATT CAAGAAGCCG CTCAGCTATC
    GGCCTTAAGG GCCCAGCTGG GTGCGCAGGC CGGGGGGGTAA GTTCTTCGGC GAGTCGATAG

61 CCGGCCAGCA CAGGGCGCCC GGCGCGCCTC GGAGCGCAAG TTCCTCGCCT TCTCCTGCCC
    GGCCGGTCGT GTCCCGCGGG CCGCGCGGAG CCTCGCGTTC AAGGAGCGGA AGAGGACGGG

121 GCTCGCTGGG CATTATGCGG CCAAGCAGCC GAGCCCCAGT CCTCCTCCTC CTCCTGCTCC
    CGAGCGACCC GTAATACGCC GGTTCGTCGG CTCGGGGTCA GGAGGAGGAG GAGGACGAGG

181 TCCGGCTCCT CCTGCGGCCC GAGCGGCTCA GCTCTCGGCA GGCGGCGGCG TTGCTCAGCC
    AGGCCGAGGA GGACGCCGGG CTCGCCGAGT CGAGAGCCGT CCGCCGCCGC AACGAGTCGG

241 GAGCGCAGAC GGGACCCTCG CAGCGAGACC TCAGCGACTC CTAAAGTCAA AAGTTGGCGG
    CTCGCGTCTG CCCTGGGAGC GTCGCTCTGG AGTCGCTGAG GATTTCAGTT TTCAACCGCC

301 CGGGCGCCGG GCTCCGCGCG CTCTCCACGG CCGCTGCCTC GCGTCGCCGC CGCAGCCAAG
    GCCCGCGGCC CGAGGCGCGC GAGAGGTGCC GGCGACGGAG CGCAGCGGCG GCGTCGGTTC

+2   M   Q   F
                                                           Start   met
                                                              ===
                                                     Kozak consensus
                                                     ========
                                                     Signal peptide
                                                     ========
361 GAGGGCAGGA GGGAGGGGGG TGGGGGCAGC GGAGGGAGGG GTGGGAAGCA CCATGCAGTT
    CTCCCGTCCT CCCTCCCCCC ACCCCCGTCG CCTCCCTCCC CACCCTTCGT GGTACGTCAA

+2 V   S   W   A   T   L   L   T   L   L   V   R   D   L   A   E   M   G   S   P
                                               signal peptide cleavage site
                                                                   =
                         Signal peptide   Prodomain
    === ===============
421 TGTATCCTGG GCCACACTGC TAACGCTCCT GGTGCGGGAC CTGGCCGAGA TGGGGAGCCC
    ACATAGGACC CGGTGTGACG ATTGCGAGGA CCACGCCCTG GACCGGCTCT ACCCCTCGGG

+2 D   A   A   A   A   V   R   K   D   R   L   H   P   R   Q   V   K   L   L   E
                                                                   Prodomain
    ==
481 AGACGCCGCG GCGGCCGTGC GCAAGGACAG GCTGCACCCG AGGCAAGTGA AATTATTAGA
    TCTGCGGCGC CGCCGGCACG CGTTCCTGTC CGACGTGGGC TCCGTTCACT TTAATAATCT

+2 T   L   S   E   Y   E   I   V   S   P   I   R   V   N   A   L   G   E   P   F
                                                                   Prodomain
    ==
541 GACCCTGAGC GAATACGAAA TCGTGTCTCC CATCCGAGTG AACGCTCTCG GAGAACCCTT
    CTGGGACTCG CTTATGCTTT AGCACAGAGG GTAGGCTCAC TTGCGAGAGC CTCTTGGGAA

+2 P   T   N   V   H   F   K   R   T   R   R   S   I   N   S   A   T   D   P   W
                                                                   Prodomain
    ==
601 TCCCACGAAC GTCCACTTCA AAAGAACGCG ACGGAGCATT AACTCTGCCA CTGACCCCTG

                                                              Prodomain

       ==

661 GCCTGCCTTC GCCTCCTCCT CTTCCTCCTC TACCTCCTCC CAGGCGCATT ACCGCCTCTC
     CGGACGGAAG CGGAGGAGGA GAAGGAGGAG ATGGAGGAGG GTCCGCGTAA TGGCGGAGAG

     +2   A   F   G   Q   Q   F   L   F   N   L   T   A   N   A   G   F   I   A   P   I
                                                              Prodomain

       ==

721 TGCCTTCGGC CAGCAGTTTC TATTTAATCT CACCGCCAAT GCCGGATTTA TCGCTCCACT
     ACGGAAGCCG GTCGTCAAAG ATAAATTAGA GTGGCGGTTA CGGCCTAAAT AGCGAGGTGA

     +2   F   T   V   T   L   L   G   T   P   G   V   N   Q   T   K   F   Y   S   E   E
                                                              Prodomain

       ==

781 GTTCACTGTC ACCCTCCTCG GGACGCCCGG GGTGAATCAG ACCAAGTTTT ATTCCGAAGA
     CAAGTGACAG TGGGAGGAGC CCTGCGGGCC CCACTTAGTC TGGTTCAAAA TAAGGCTTCT

     +2   E   A   E   L   K   H   C   F   Y   K   G   Y   V   N   T   N   S   E   H   T
                                            Prodomain

       ==

841 GGAAGCGGAA CTCAAGCACT GTTTCTACAA AGGCTATGTC AATACCAACT CCGAGCACAC
     CCTTCGCCTT GAGTTCGTGA CAAAGATGTT TCCGATACAG TTATGGTTGA GGCTCGTGTG

     +2   A   V   I   S   L   C   S   G   M   L   G   T   F   R   S   H   D   G   D   Y
          Prodomain

       ==

901 GGCCGTCATC AGCCTCTGCT CAGGAATGCT GGGCACATTC CGGTCTCATG ATGGGGATTA
     CCGGCAGTAG TCGGAGACGA GTCCTTACGA CCCGTGTAAG GCCAGAGTAC TACCCCTAAT

     +2   F   I   E   P   L   Q   S   M   D   E   Q   E   D   E   E   E   Q   N   K   P
          Prodomain

       ==

961 TTTTATTGAA CCACTACAGT CTATGGATGA ACAAGAAGAT GAAGAGGAAC AAAACAAACC
     AAAATAACTT GGTGATGTCA GATACCTACT TGTTCTTCTA CTTCTCCTTG TTTTGTTTGG

     +2   H   I   I   Y   R   R   S   A   P   Q   R   E   P   S   T   G   R   H   A   C
          Prodomain

       ==

1021 CCACATCATT TATAGGCGCA GCGCCCCCCA GAGAGAGCCC TCAACAGGAA GGCATGCATG
     GGTGTAGTAA ATATCCGCGT CGCGGGGGGT CTCTCTCGGG AGTTGTCCTT CCGTACGTAC

     +2   D   T   S   E   H   K   N   R   H   S   K   D   K   K   K   T   R   A   R   K
          Prodomain

       ==

1081 TGACACCTCA GAACACAAAA ATAGGCACAG TAAAGACAAG AAGAAAACCA GAGCAAGAAA
     ACTGTGGAGT CTTGTGTTTT TATCCGTGTC ATTTCTGTTC TTCTTTTGGT CTCGTTCTTT

     +2   W   G   E   R   I   N   L   A   G   D   V   A   A   L   N   S   G   L   A   T
          Prodomain

       ==

1141 ATGGGGAGAA AGGATTAACC TGGCTGGTGA CGTAGCAGCA TTAAACAGCG GCTTAGCAAC
     TACCCCTCTT TCCTAATTGG ACCGACCACT GCATCGTCGT AATTTGTCGC CGAATCGTTG

```
-2   E   A   F   S   A   Y   G   N   K   T   D   N   T   R   E   K   R   T   H   F
     Prodomain
     ===========================================================================
1201 AGAGGCATTT TCTGCTTATG GTAATAAGAC GGACAACACA AGAGAAAAGA GGACCCACAG
     TCTCCGTAAA AGACGAATAC CATTATTCTG CCTGTTGTGT TCTCTTTTCT CCTGGGTGTC

 +2   R   T   K   R   F   L   S   Y   P   R   F   V   E   V   L   V   V   A   D   N
     Furin Cleavage site

     Prodomain                                    Metalloproteinase  domain
     ===========================================================================
1261 AAGGACAAAA CGTTTTTTAT CCTATCCACG GTTTGTAGAA GTCTTGGTGG TGGCAGACAA
     TTCCTGTTTT GCAAAAAATA GGATAGGTGC CAAACATCTT CAGAACCACC ACCGTCTGTT

 +2   R   M   V   S   Y   H   G   E   N   L   Q   H   Y   I   L   T   L   M   S   I
                                      Metalloproteinase  domain
     ===========================================================================
1321 CAGAATGGTT TCATACCATG GAGAAAACCT TCAACACTAT ATTTTAACTT TAATGTCAAT
     GTCTTACCAA AGTATGGTAC CTCTTTTGGA AGTTGTGATA TAAAATTGAA ATTACAGTTA

 +2   V   A   S   I   Y   K   D   P   S   I   G   N   L   I   N   I   V   I   V   N
                                      Metalloproteinase  domain
     ===========================================================================
1381 TGTAGCCTCT ATCTATAAAG ACCCAAGTAT TGGAAATTTA ATTAATATTG TTATTGTGAA
     ACATCGGAGA TAGATATTTC TGGGTTCATA ACCTTTAAAT TAATTATAAC AATAACACTT

 +2   L   I   V   I   H   N   E   Q   D   G   P   S   I   S   F   N   A   Q   T   T
                                      Metalloproteinase  domain
     ===========================================================================
1441 CTTAATTGTG ATTCATAATG AACAGGATGG GCCTTCCATA TCTTTTAATG CTCAGACAAC
     GAATTAACAC TAAGTATTAC TTGTCCTACC CGGAAGGTAT AGAAAATTAC GAGTCTGTTG

 +2   L   K   N   F   C   Q   W   Q   H   S   K   N   S   P   G   G   I   H   H   D
                                      Metalloproteinase  domain
     ===========================================================================
1501 ATTAAAAAAC TTTTGCCAGT GGCAGCATTC GAAGAACAGT CCAGGTGGAA TCCATCATGA
     TAATTTTTTG AAAACGGTCA CCGTCGTAAG CTTCTTGTCA GGTCCACCTT AGGTAGTACT

 +2   T   A   V   L   L   T   R   Q   D   I   C   R   A   H   D   K   C   D   T   I
     Metalloproteinase  domain
     ===========================================================================
1561 TACTGCTGTT CTCTTAACAA GACAGGATAT CTGCAGAGCT CACGACAAAT GTGATACCTT
     ATGACGACAA GAGAATTGTT CTGTCCTATA GACGTCTCGA GTGCTGTTTA CACTATGGAA

 +2   G   L   A   E   L   G   T   I   C   D   P   Y   R   S   C   S   I   S   E   D
     Metalloproteinase  domain
     ===========================================================================
1621 AGGCCTGGCT GAACTGGGAA CCATTTGTGA TCCCTATAGA AGCTGTTCTA TTAGTGAAGA
     TCCGGACCGA CTTGACCCTT GGTAAACACT AGGGATATCT TCGACAAGAT AATCACTTCT
```

```
 +2    S   G   L   S   T   A   F   T   I   A   H   E   L   G   H   V   F   N   M   F
                                                              Zinc  Binding  Domain
                                    =====================================
             Metalloproteinase  domain
             ===========================================================
1681   TAGTGGATTG AGTACAGCTT TTACGATCGC CCATGAGCTG GGCCATGTGT TTAACATGCC
       ATCACCTAAC TCATGTCGAA AATGCTAGCG GGTACTCGAC CCGGTACACA AATTGTACGG


   +2   H   D   D   N   N   K   C   K   E   E   G   V   K   S   P   Q   H   V   M   A
        Zinc  Binding  Domain
        ==========
        Metalloproteinase  domain
        ==========================================================================
1741   TCATGATGAC AACAACAAAT GTAAAGAAGA AGGAGTTAAG AGTCCCCAGC ATGTCATGGC
       AGTACTACTG TTGTTGTTTA CATTTCTTCT TCCTCAATTC TCAGGGGTCG TACAGTACCG


   +2   P   T   L   N   F   Y   T   N   P   W   M   W   S   K   C   S   R   K   Y   I
                              Heparin  Binding  Motif
                              =============
             Metalloproteinase  domain              Heparin  Binding  Motif
             ==========================              =================
1801   TCCAACACTG AACTTCTACA CCAACCCCTG GATGTGGTCA AAGTGTAGTC GAAAATATAT
       AGGTTGTGAC TTGAAGATGT GGTTGGGGAC CTACACCAGT TTCACATCAG CTTTTATATA


   +2   T   E   F   L   D   T   G   Y   G   E   C   L   L   N   E   P   E   S   R   P
1861   CACTGAGTTT TTAGACACTG GTTATGGCGA GTGTTTGCTT AACGAACCTG AATCCAGACC
       GTGACTCAAA AATCTGTGAC CAATACCGCT CACAAACGAA TTGCTTGGAC TTAGGTCTGG


   +2   Y   P   L   P   V   Q   L   P   G   I   L   Y   N   V   N   K   Q   C   E   L
                                                              Disintegrin  domain
                           ============================================================
1921   CTACCCTTTG CCTGTCCAAC TGCCAGGCAT CCTTTACAAC GTGAATAAAC AATGTGAATT
       GATGGGAAAC GGACAGGTTG ACGGTCCGTA GGAAATGTTG CACTTATTTG TTACACTTAA


   +2   I   F   G   P   G   S   Q   V   C   P   Y   M   M   Q   C   R   R   L   W   C
                                                              Disintegrin  domain
             ==============================================================
1981   GATTTTTGGA CCAGGTTCTC AGGTGTGCCC ATATATGATG CAGTGCAGAC GGCTCTGGTG
       CTAAAAACCT GGTCCAAGAG TCCACACGGG TATATACTAC GTCACGTCTG CCGAGACCAC


   +2   N   N   V   N   G   V   H   K   G   C   R   T   Q   H   T   P   W   A   D   G
                 Disintegrin  domain
             ===========================================================
2041   CAATAACGTC AATGGAGTAC ACAAAGGCTG CCGGACTCAG CACACACCCT GGGCCGATGG
       GTTATTGCAG TTACCTCATG TGTTTCCGAC GGCCTGAGTC GTGTGTGGGA CCCGGCTACC


   +2   T   E   C   E   P   G   K   H   C   K   Y   G   F   C   V   P   K   E   M   D
        Disintegrin  domain
             ===========================================================
2101   GACGGAGTGC GAGCCTGGAA AGCACTGCAA GTATGGATTT TGTGTTCCCA AAGAAATGGA
       CTGCCTCACG CTCGGACCTT TCGTGACGTT CATACCTAAA ACACAAGGGT TTCTTTACCT
```

```
          V   P   V   T   D   G   S   W   G   S   W   S   F   F   G   T   C   S   R   T
          Disintegrin  domain                                                    TSP1
          ================            =================================================
     2161 TGTCCCCGTG ACAGATGGAT CCTGGGGAAG TTGGAGTCCC TTTGGAACCT GCTCCAGAAC
          ACAGGGGCAC TGTCTACCTA GGACCCCTTC AACCTCAGGG AAACCTTGGA CGAGGTCTTG


       +2 C   G   G   G   I   K   T   A   I   R   E   C   N   R   P   E   P   K   N   G
                                                                   TSP1
          ================================================================================
     2221 ATGTGGAGGG GGCATCAAAA CAGCCATTCG AGAGTGCAAC AGACCAGAAC CAAAAAATGG
          TACACCTCCC CCGTAGTTTT GTCGGTAAGC TCTCACGTTG TCTGGTCTTG GTTTTTTACC


       +2 G   K   Y   C   V   G   R   R   M   K   F   K   S   C   N   T   E   P   C   L
          TSP1                                                         Spacer Region
          ================================================================================
     2281 TGGAAAATAC TGTGTAGGAC GTAGAATGAA ATTTAAGTCC TGCAACACGG AGCCATGTCT
          ACCTTTTATG ACACATCCTG CATCTTACTT TAAATTCAGG ACGTTGTGCC TCGGTACAGA


       +2 K   Q   K   R   D   F   R   D   E   Q   C   A   H   F   D   G   K   H   F   N
                                                                   Spacer Region
          ================================================================================
     2341 CAAGCAGAAG CGAGACTTCC GAGATGAACA GTGTGCTCAC TTTGACGGGA AGCATTTTAA
          GTTCGTCTTC GCTCTGAAGG CTCTACTTGT CACACGAGTG AAACTGCCCT TCGTAAAATT


       +2 I   N   G   L   L   P   N   V   R   W   V   P   K   Y   S   G   I   L   M   K
                                                                   Spacer Region
          ================================================================================
     2401 CATCAACGGT CTGCTTCCCA ATGTGCGCTG GGTCCCTAAA TACAGTGGAA TTCTGATGAA
          GTAGTTGCCA GACGAAGGGT TACACGCGAC CCAGGGATTT ATGTCACCTT AAGACTACTT


       +2 D   R   C   K   L   F   C   R   V   A   G   N   T   A   Y   Y   Q   L   R   D
                                                                   Spacer Region
          ================================================================================
     2461 GGACCGGTGC AAGTTGTTCT GCAGAGTGGC AGGGAACACA GCCTACTATC AGCTTCGAGA
          CCTGGCCACG TTCAACAAGA CGTCTCACCG TCCCTTGTGT CGGATGATAG TCGAAGCTCT


       +2 R   V   I   D   G   T   P   C   G   Q   D   T   N   D   I   C   V   Q   G   L
                                                                   Spacer Region
          ================================================================================
     2521 CAGAGTGATA GATGGAACTC CTTGTGGCCA GGACACAAAT GATATCTGTG TCCAGGGCCT
          GTCTCACTAT CTACCTTGAG GAACACCGGT CCTGTGTTTA CTATAGACAC AGGTCCCGGA


       +2 C   R   Q   A   G   C   D   H   V   L   N   S   K   A   R   R   D   K   C   G
                                                                   Spacer Region
          ================================================================================
     2581 TTGCCGGCAA GCTGGATGCG ATCATGTTTT AAACTCAAAA GCCCGGAGAG ATAAATGTGG
          AACGGCCGTT CGACCTACGC TAGTACAAAA TTTGAGTTTT CGGGCCTCTC TATTTACACC


       +2 V   C   G   G   D   N   S   S   C   K   T   V   A   G   T   F   N   T   V   H
                                                                   Spacer Region
          ================================================================================
     2641 GGTTTGTGGT GGCGATAATT CTTCATGCAA AACAGTGGCA GGAACATTTA ATACAGTACA
          CCAAACACCA CCGCTATTAA GAAGTACGTT TTGTCACCGT CCTTGTAAAT TATGTCATGT
```

```
       +2   Y  G  Y   N  T  V  V   R  I  P   A  G  A   T  N  I  D   V  R  C
                                                        Spacer  Region
            ================================================================
      2701  TTATGGTTAC AATACTGTGG TCCGAATTCC AGCTGGTGCT ACCAATATTG ATGTGCGGCA
            AATACCAATG TTATGACACC AGGCTTAAGG TCGACCACGA TGGTTATAAC TACACGCCGT


       +2   H  S  F   S  G  E  T   D  D  D   N  Y  L   A  L  S  S   S  K  G
                                                        Spacer  Region
            ================================================================
      2761  GCACAGTTTC TCAGGGGAAA CAGACGATGA CAACTACTTA GCTTTATCAA GCAGTAAAGG
            CGTGTCAAAG AGTCCCCTTT GTCTGCTACT GTTGATGAAT CGAAATAGTT CGTCATTTCC


       +2   E  F  L   L  N  G  N   F  V  V   T  M  A   K  R  E  I   R  I  G
                                                        Spacer  Region
            ================================================================
      2821  TGAATTCTTG CTAAATGGAA ACTTTGTTGT CACAATGGCC AAAAGGGAAA TTCGCATTGG
            ACTTAAGAAC GATTTACCTT TGAAACAACA GTGTTACCGG TTTTCCCTTT AAGCGTAACC


       +2   N  A  V   V  E  Y  S   G  S  E   T  A  V   E  R  I  N   S  T  D
                      Spacer Region
            ================================================================
      2881  GAATGCTGTG GTAGAGTACA GTGGGTCCGA GACTGCCGTA GAAAGAATTA ACTCAACAGA
            CTTACGACAC CATCTCATGT CACCCAGGCT CTGACGGCAT CTTTCTTAAT TGAGTTGTCT


       +2   R  I  E   Q  E  L  L   L  Q  V   L  S  V   G  K  L  Y   N  P  D
            Spacer Region
            ================================================================
      2941  TCGCATTGAG CAAGAACTTT TGCTTCAGGT TTTGTCGGTG GGAAAGTTGT ACAACCCCGA
            AGCGTAACTC GTTCTTGAAA ACGAAGTCCA AAACAGCCAC CCTTTCAACA TGTTGGGGCT


       +2   V  R  Y   S  F  N  I   P  I  E   D  K  P   Q  Q  F  Y   W  N  S
            Spacer Region
            ================================================================
      3001  TGTACGCTAT TCTTTCAATA TTCCAATTGA AGATAAACCT CAGCAGTTTT ACTGGAACAG
            ACATGCGATA AGAAAGTTAT AAGGTTAACT TCTATTTGGA GTCGTCAAAA TGACCTTGTC


       +2   H  G  P   W  Q  A  C   S  K  P   C  Q  G   E  R  K  R   K  L  V
            Spacer Region
            ================================================================
      3061  TCATGGGCCA TGGCAAGCAT GCAGTAAACC CTGCCAAGGG GAACGGAAAC GAAAACTTGT
            AGTACCCGGT ACCGTTCGTA CGTCATTTGG GACGGTTCCC CTTGCCTTTG CTTTTGAACA


       +2   C  T  R   E  S  D  Q   L  T  V   S  D  Q   R  C  D  R   L  P  C
            Spacer Region
            ================================================================
      3121  TTGCACCAGG GAATCTGATC AGCTTACTGT TTCTGATCAA AGATGCGATC GGCTGCCCCA
            AACGTGGTCC CTTAGACTAG TCGAATGACA AAGACTAGTT CTACGCTAG CCGACGGGGT


       +2   P  G  H   I  T  E  P   C  G  T   D  C  D   L  R  W  H   V  A  S
            Spacer Region
            ================================================================
      3181  GCCTGGACAC ATTACTGAAC CCTGTGGTAC AGACTGTGAC CTGAGGTGGC ATGTTGCCAG
            CGGACCTGTG TAATGACTTG GGACACCATG TCTGACACTG GACTCCACCG TACAACGGTC
```

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    +2   R  S  E   C  S  A  Q   C  G  L   G  Y  R   T  L  D   I  Y  C  A
         Spacer Region
         =====================================================================
3241  CAGGAGTGAA TGTAGTGCCC AGTGTGGCTT GGGTTACCGC ACATTGGACA TCTACTGTGC
      GTCCTCACTT ACATCACGGG TCACACCGAA CCCAATGGCG TGTAACCTGT AGATGACACG


    +2   K  Y  S   R  L  D  G   K  T  E   K  V  D   D  G  F   C  S  S  H
         Spacer Region
         =====================================================================
3301  CAAATATAGC AGGCTGGATG GGAAGACTGA GAAGGTTGAT GATGGTTTTT GCAGCAGCCA
      GTTTATATCG TCCGACCTAC CCTTCTGACT CTTCCAACTA CTACCAAAAA CGTCGTCGGT


    +2   P  K  F   S  N  R  E   K  C  S   G  E  C   N  T  G   G  W  R  Y
         Spacer Region
         =====================================================================
3361  TCCCAAACCA AGCAACCGTG AAAAATGCTC AGGGGAATGT AACACGGGTG GCTGGCGCTA
      AGGGTTTGGT TCGTTGGCAC TTTTTACGAG TCCCCTTACA TTGTGCCCAC CGACCGCGAT


    +2   S  A  W   T  E  C  S   K  S  C   D  G  G   T  Q  R   R  R  A  I
         Spacer Region                                               TSP2
         =====================================================================
3421  TTCTGCCTGG ACTGAATGTT CAAAAAGCTG TGACGGTGGG ACCCAGAGGA GAAGGGCTAT
      AAGACGGACC TGACTTACAA GTTTTTCGAC ACTGCCACCC TGGGTCTCCT CTTCCCGATA


    +2   C  V  N   T  R  N  D   V  L  D   D  S  K   C  T  H   Q  E  K  V
                                   TSP2
         =====================================================================
3481  TTGTGTCAAT ACCCGAAATG ATGTACTGGA TGACAGCAAA TGCACACATC AAGAGAAAGT
      AACACAGTTA TGGGCTTTAC TACATGACCT ACTGTCGTTT ACGTGTGTAG TTCTCTTTCA


    +2   T  I  Q   R  C  S  E   F  P  C   P  Q  W   K  S  G   D  W  S  E
         TSP2                                                        TSP3
         ==================================     ==============================
3541  TACCATTCAG AGGTGCAGTG AGTTCCCTTG TCCACAGTGG AAATCTGGAG ACTGGTCAGA
      ATGGTAAGTC TCCACGTCAC TCAAGGGAAC AGGTGTCACC TTTAGACCTC TGACCAGTCT


    +2   C  L  V   T  C  G  K   G  H  K   H  R  Q   V  W  C   Q  F  G  E
                                                                  TSP3
         =====================================================================
3601  GTGCTTGGTC ACCTGTGGAA AAGGGCATAA GCACCGCCAG GTCTGGTGTC AGTTTGGTGA
      CACGAACCAG TGGACACCTT TTCCCGTATT CGTGGCGGTC CAGACCACAG TCAAACCACT


    +2   D  R  L   N  D  R  M   C  D  F   E  T  K   P  T  S   M  Q  T  C
         TSP3
         =====================================================================
3661  AGATCGATTA AATGATAGAA TGTGTGACCC TGAGACCAAG CCAACATCTA TGCAGACTTG
      TCTAGCTAAT TTACTATCTT ACACACTGGG ACTCTGGTTC GGTTGTAGAT ACGTCTGAAC


    +2   Q  Q  F   E  C  A  S   W  Q  A   G  P  W   G  Q  C   S  V  T  C
         TSP3                                                        TSP4
         ==================     ==============================================
3721  TCAGCAGCCG GAATGTGCAT CCTGGCAGGC GGGTCCCTGG GGACAGTGCA GTGTCACTTG
      AGTCGTCGGC CTTACACGTA GGACCGTCCG CCCAGGGACC CCTGTCACGT CACAGTGAAC
```

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+1        G  Q  G   Y  Q  L  R   A  V  K   C  I  I   G  T  Y   M  S  V  V
                                                   TSP4

          =========================================================
3781   TGGACAGGGA TACCAGCTAA GAGCAGTGAA ATGCATCATT GGGACTTATA TGTCAGTGGT
       ACCTGTCCCT ATGGTCGATT CTCGTCACTT TACGTAGTAA CCCTGAATAT ACAGTCACCA


   +2     D  D  N   D  C  N  A   A  T  R   P  T  D   T  Q  D   C  E  L  F
       TSP4

          =========================================================
3841   AGATGACAAT GACTGTAATG CAGCAACTAG ACCAACTGAT ACCCAGGACT GTGAATTACC
       TCTACTGTTA CTGACATTAC GTCGTTGATC TGGTTGACTA TGGGTCCTGA CACTTAATGG


   +2     S  C  H   P  P  P  A   A  P  E   T  R  R   S  T  Y   S  A  P  R
       TSP4
       =======

3901   ATCATGTCAT CCTCCCCCAG CTGCCCCGGA AACGAGGAGA AGCACATACA GTGCACCAAG
       TAGTACAGTA GGAGGGGGTC GACGGGGCCT TTGCTCCTCT TCGTGTATGT CACGTGGTTC


   +2     T  Q  W   R  F  G  S   W  T  P   C  S  A   T  C  G   K  G  T  R
                                                              TSP5

          =========================================================
3961   AACCCAGTGG CGATTTGGGT CTTGGACCCC ATGCTCAGCC ACTTGTGGGA AAGGTACCCG
       TTGGGTCACC GCTAAACCCA GAACCTGGGG TACGAGTCGG TGAACACCCT TTCCATGGGC


   +2     M  R  Y   V  S  C  R   D  E  N   G  S  V   A  D  E   S  A  C  A
                 TSP5

          =========================================================
4021   GATGAGATAC GTCAGCTGCC GAGATGAGAA TGGCTCTGTG GCTGACGAGA GTGCCTGTGC
       CTACTCTATG CAGTCGACGG CTCTACTCTT ACCGAGACAC CGACTGCTCT CACGGACACG


   +2     T  L  P   R  P  V  A   K  E  E   C  S  V   T  P  C   G  Q  W  K
       TSP5                                                       TSP6

          =========================================================
4081   TACCCTGCCT AGACCAGTGG CAAAGGAAGA ATGTTCTGTG ACACCCTGTG GGCAATGGAA
       ATGGGACGGA TCTGGTCACC GTTTCCTTCT TACAAGACAC TGTGGGACAC CCGTTACCTT


   +2     A  L  D   W  S  S  C   S  V  T   C  G  Q   G  R  A   T  R  Q  V
                                                              TSP6

          =========================================================
4141   GGCCTTGGAC TGGAGCTCTT GCTCTGTGAC CTGTGGGCAA GGTAGGGCAA CCCGGCAAGT
       CCGGAACCTG ACCTCGAGAA CGAGACACTG GACACCCGTT CCATCCCGTT GGGCCGTTCA


   +2     M  C  V   N  Y  S  D   H  V  I   D  R  S   E  C  D   Q  D  Y  I
                 TSP6

          =========================================================
4201   GATGTGTGTC AACTACAGTG ACCACGTGAT CGATCGGAGT GAGTGTGACC AGGATTATAT
       CTACACACAG TTGATGTCAC TGGTGCACTA GCTAGCCTCA CTCACACTGG TCCTAATATA


   +2     P  E  T   D  Q  D  C   S  M  S   P  C  P   Q  R  T   P  D  S  G
       TSP6

          ====================================================
4261   CCCAGAAACT GACCAGGACT GTTCCATGTC ACCATGCCCT CAAAGGACCC CAGACAGTGG
       GGGTCTTTGA CTGGTCCTGA CAAGGTACAG TGGTACGGGA GTTTCCTGGG GTCTGTCACC
```

```
      +2   L   A   Q   H   P   F   Q   N   E   D   Y   R   F   R   S   A   S   P   S   F
    4321  CTTAGCTCAG  CACCCCTTCC  AAAATGAGGA  CTATCGTCCC  CGGAGCGCCA  GCCCCAGCCG
          GAATCGAGTC  GTGGGGAAGG  TTTTACTCCT  GATAGCAGGG  GCCTCGCGGT  CGGGGTCGGC


      +2   T   H   V   L   G   G   N   Q   W   R   T   G   P   W   G   A   C   S   S   T
                                                                              TSP7
                       ==========================================================
    4381  CACCCATGTG  CTCGGTGGAA  ACCAGTGGAG  AACTGGCCCC  TGGGGAGCAT  GTTCCAGTAC
          GTGGGTACAC  GAGCCACCTT  TGGTCACCTC  TTGACCGGGG  ACCCCTCGTA  CAAGGTCATG


      +2   C   A   G   G   S   Q   R   V   V   V   C   Q   D   E   N   G   Y   T   A
                                                               TSP7
          ===============================================================================
    4441  CTGTGCTGGC  GGATCCCAGC  GGCGTGTTGT  TGTATGTCAG  GATGAAAATG  GATACACCGC
          GACACGACCG  CCTAGGGTCG  CCGCACAACA  ACATACAGTC  CTACTTTTAC  CTATGTGGCG


      +2   N   D   C   V   E   R   I   K   P   D   E   Q   R   A   C   E   S   G   P   C
          TSP7
          ===============================================================================
    4501  AAACGACTGT  GTGGAGAGAA  TAAAACCTGA  TGAGCAAAGA  GCCTGTGAAT  CCGGCCCTTG
          TTTGCTGACA  CACCTCTCTT  ATTTTGGACT  ACTCGTTTCT  CGGACACTTA  GGCCGGGAAC


      +2   P   Q   W   A   Y   G   N   W   G   E   C   T   K   L   C   G   G   I   R
          TSP7                                                               TSP8
          ==         ===============================================================
    4561  TCCTCAGTGG  GCTTATGGCA  ACTGGGGAGA  GTGCACTAAG  CTGTGTGGTG  GAGGCATAAG
          AGGAGTCACC  CGAATACCGT  TGACCCCTCT  CACGTGATTC  GACACACCAC  CTCCGTATTC


      +2   T   R   L   V   V   C   Q   R   S   N   G   E   R   F   P   D   L   S   C   E
                                        TSP8
          ===============================================================================
    4621  AACAAGACTG  GTGGTCTGTC  AGCGGTCCAA  CGGTGAACGG  TTTCCAGATT  TGAGCTGTGA
          TTGTTCTGAC  CACCAGACAG  TCGCCAGGTT  GCCACTTGCC  AAAGGTCTAA  ACTCGACACT


      +2   I   L   D   K   P   P   D   R   E   Q   C   N   T   H   A   C   P   H   D   A
          TSP8
          ============================================================================
    4681  AATTCTTGAT  AAACCTCCCG  ATCGTGAGCA  GTGTAACACA  CATGCTTGTC  CACACGACGC
          TTAAGAACTA  TTTGGAGGGC  TAGCACTCGT  CACATTGTGT  GTACGAACAG  GTGTGCTGCG


      +2   A   W   S   T   G   P   W   S   S   C   S   V   S   C   G   R   G   H   K   Q
                                                                              TSP9
                     =================================================================
    4741  TGCATGGAGT  ACTGGCCCTT  GGAGCTCGTG  TTCTGTCTCT  TGTGGTCGAG  GGCATAAACA
          ACGTACCTCA  TGACCGGGAA  CCTCGAGCAC  AAGACAGAGA  ACACCAGCTC  CCGTATTTGT


      +2   R   N   V   Y   C   M   A   K   D   G   S   H   L   E   S   D   Y   C   K   H
                                    TSP9
          ===============================================================================
    4801  ACGAAATGTT  TACTGCATGG  CAAAAGATGG  AAGCCATTTA  GAAAGTGATT  ACTGTAAGCA
          TGCTTTACAA  ATGACGTACC  GTTTTCTACC  TTCGGTAAAT  CTTTCACTAA  TGACATTCGT


      +2   L   A   K   P   H   G   H   R   K   C   R   G   G   R   C   P   K   W   K   A
          TSP9                                                               TSP10
```

```
       ===============================================          ========
4861   CCTGGCTAAG CCACATGGGC ACAGAAAGTG CCGAGGAGGA AGATGCCCCA AATGGAAAGC
       GGACCGATTC GGTGTACCCG TGTCTTTCAC GGCTCCTCCT TCTACGGGGT TTACCTTTCG

  +2    G   A   W   S   Q   C   S   V   S   C   G   R   G   V   Q   Q   R   H   V   G
                                                                    TSP10
       =======================================================================
4921   TGGCGCTTGG AGTCAGTGCT CTGTGTCCTG TGGCCGAGGC GTACAGCAGA GGCATGTGGG
       ACCGCGAACC TCAGTCACGA GACACAGGAC ACCGGCTCCG CATGTCGTCT CCGTACACCC

  +2    C   Q   I   G   T   H   K   I   A   R   E   T   E   C   N   P   Y   T   R   F
               TSP10
       =======================================================================
4981   CTGTCAGATC GGAACACACA AAATAGCCAG AGAGACCGAG TGCAACCCAT ACACCAGACC
       GACAGTCTAG CCTTGTGTGT TTTATCGGTC TCTCTGGCTC ACGTTGGGTA TGTGGTCTGG

  +2    E   S   E   R   D   C   Q   G   P   R   C   P   L   Y   T   W   R   A   E   E
       TSP10                                                            TSP11
       =========================================          =====
5041   GGAGTCGGAA CGCGACTGCC AAGGCCCACG GTGTCCCCTC TACACTTGGA GGGCAGAGGA
       CCTCAGCCTT GCGCTGACGG TTCCGGGTGC CACAGGGGAG ATGTGAACCT CCCGTCTCCT

  +2    W   Q   E   C   T   K   T   C   G   E   G   S   R   Y   R   K   V   V   C   V
                                                                    TSP11
       =======================================================================
5101   ATGGCAAGAA TGCACCAAGA CCTGCGGCGA AGGCTCCAGG TACCGCAAGG TGGTGTGTGT
       TACCGTTCTT ACGTGGTTCT GGACGCCGCT TCCGAGGTCC ATGGCGTTCC ACCACACACA

  +2    D   D   N   K   N   E   V   H   G   A   R   C   D   V   S   K   R   P   V   D
                   TSP11
       =======================================================================
5161   GGATGACAAC AAAAACGAGG TGCATGGGGC ACGCTGTGAC GTGAGCAAGC GGCCGGTGGA
       CCTACTGTTG TTTTTGCTCC ACGTACCCCG TGCGACACTG CACTCGTTCG CCGGCCACCT

  +2    R   E   S   C   S   L   Q   P   C   E   Y   V   W   I   T   G   E   W   S   E
       TSP11
       ================================
5221   CCGTGAAAGC TGTAGTTTGC AACCCTGCGA GTATGTCTGG ATCACAGGAG AATGGTCAGA
       GGCACTTTCG ACATCAAACG TTGGGACGCT CATACAGACC TAGTGTCCTC TTACCAGTCT

  +2    V   P   S   W   E   L   *
                      ·Termination   codon
                  ====
5281   GGTACCGTCC TGGGAACTGT AACCATCGTC AGCTCAGCCA TGGCCTGAGA GTGGCAGAGG
       CCATGGCAGG ACCCTTGACA TTGGTAGCAG TCGAGTCGGT ACCGGACTCT CACCGTCTCC

5341   GATGAGTGGA GGGATGAGTG CAGGAATGTG GGAGACTTGA GGCTACCCGC CCGATTTGCC
       CTACTCACCT CCCTACTCAC GTCCTTACAC CCTCTGAACT CCGATGGGCG GGCTAAACGG

5401   ACTGTGAACT GTGTGTTTTC TGACAAGTCC TCAGCTTTCC CAAGCTAGAA TTCCTTGTAT
       TGACACTTGA CACACAAAAG ACTGTTCAGG AGTCGAAAGG GTTCGATCTT AAGGAACATA

5461   GCAAAGCGGG AGAGATGTAA GAGATGGTCT CTAAGTCCCT TCAGGTCTAC ATTCTGTGAT
       CGTTTCGCCC TCTCTACATT CTCTACCAGA GATTCAGGGA AGTCCAGATG TAAGACACTA
```

```
5521   TCACCTTGAT GTCCTATTGG CATAAAGAAG AAATTATTAC AGGGGCTGCA AACTCATAGG
       AGTGGAACTA CAGGATAACC GTATTTCTTC TTTAATAATG TCCCCGACGT TTGAGTATCC

5581   ATGCTGTGAG GTGCCTGAAG ACAGTTAAGT ATAAGAAAAT ATTGTAGTGC CAGGGATACA
       TACGACACTC CACGGACTTC TGTCAATTCA TATTCTTTTA TAACATCACG GTCCCTATGT

5641   ACAAGGAGAG ATGGCAACTG TGACAAACTA GCACATGCTG TGTGAAGGGA GCAGAATCTC
       TGTTCCTCTC TACCGTTGAC ACTGTTTGAT CGTGTACGAC ACACTTCCCT CGTCTTAGAG

5701   TTTCACTCCA GCTGTGGCCA TGCAGAAATG TGGTCTAGCG TTACCAGACC TGATTTTTCA
       AAAGTGAGGT CGACACCGGT ACGTCTTTAC ACCAGATCGC AATGGTCTGG ACTAAAAAGT

5761   AGAGAGGCTA AAAATCTGGA CTAGTATGTG AGATTTCCTA ACTTGAAAAT GGGGGCTGAA
       TCTCTCCGAT TTTTAGACCT GATCATACAC TCTAAAGGAT TGAACTTTTA CCCCCGACTT

5821   ATTTTTGGTT TTAAAACATT GTAAGGGGCA AACAAACCCC TTTCATGAAC CAGATGTGTT
       TAAAAACCAA AATTTTGTAA CATTCCCCGT TTGTTTGGGG AAAGTACTTG GTCTACACAA

5881   GTGCCTGTTT AACAAACAGC TTCAGAGGAA GAAAATAATT TTCTATAATA TCCGAAGTAT
       CACGGACAAA TTGTTTGTCG AAGTCTCCTT CTTTTATTAA AAGATATTAT AGGCTTCATA

5941   CTCAAGTACC ATTTTTTCAT ATATCTTCCT GTGCACAATG CTTATCTAGA CCCTTTTTAA
       GAGTTCATGG TAAAAAAGTA TATAGAAGGA CACGTGTTAC GAATAGATCT GGGAAAAATT

       PolyA Site
       ======
6001   TGGTAATAAA CCAGTAGTAA TCAT
       ACCATTATTT GGTCATCATT AGTA
```
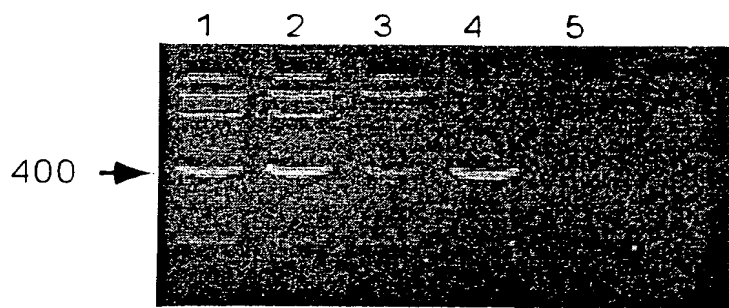
Fig. 4

Metalloproteinase Domain Alignment of TS-SI v. ADAMTS Family

Percent Homology (SI vs)

	Sim	Ident
	62	46
	58	44
	63	50
	62	49
	52	33

```
301                                                         360
hADAMTS-4  (AB014588)  (212)  REASLSRFVETLMVADUKMAAFHG-AGLKRYLMVMAAAKAMKHPMIRNPMSLVVMRLV
hADAMTS-5  (AF142099)  (261)  RSISRARQVMLLLVAMASMARLMG-RGLQHYLMMLASIANRMYSHAMIENHMRMAVVKVV
hADAMTS-1  (AF060152)  (235)  REVSSHRMVMTMLVAMQSMAMFHM-SMIKHVMLMMLFSMMARMYKHPMIRNSMSEVVVKIL
hADAMTS-8  (AF060153)  (214)  REMSEARMVMTLMVADMASMAAFMG-ADMQNMIMLMSMAARIMKHPMIKNSMNLMMVMVL
hADAMTS-2  (AJ003125)  (260)  HAADDDYNMLMVLMGVMDSMVQEHMQEHMMQKYEMMMNMVNEMMHDESMMGAHMNMVMMMII
nADAMTS-SI            (287)  REMSYPREVMVMMVADMNRMVSMMHS-ENMOHYMMLMSMVASMMKMDESIGNMMNMMVNLI
Consensus            (301)  RF S   RFVETLLVAD SMA FHGK GLQHYLLTLMSIAARIYKHPSI N INLVVK
                              361                                              420

hADAMTS-4  (AB014588)  (271)  MMGSGEEGBQVGP-SAAQTMRSFMAMQRGLNTMEDSDPMMMTMLFMMQDLGGVS-TMMD
hADAMTS-5  (AF142099)  (320)  VMMGDKDKSLEVSK-NAATTMMNFMKMQHQHNQLGDDHEEHYMAMLFMMEDMMGHH-SMD
hADAMTS-1  (AF060152)  (294)  VMMDEQKGPEVMS-NARLTMRYFMNMQKQHNPMSMRDAEHYMTAMTMFMMKQDMCGSQ-TMD
hADAMTS-8  (AF060153)  (273)  MMEDMKWMGMEVSD-NMMLMIHMNFMNMQRRFNQMSDRHPMHYMMTAMMMMNFGGQEMLMMD
hADAMTS-2  (AJ003125)  (320)  MMSYGKSMSLMEIGNPMSQSMMNVMRMAYLQMKMDTGHDEMMMHMMFMMKMQDFGPSG---
nADAMTS-SI            (346)  VMMNEQDGMSMSF-NAQTTMMMNFMOMHSKNSMGG---IMHMTMMTMMMMMGRAHDKMMD
Consensus            (361)  VL DE  GPEVS GNAA TLRNFC WQ   N P D H EHYDTAILLTRQDLCG   G CD
                              421                                              480

hADAMTS-4  (AB014588)  (329)  TMGMADVGTMMMDMARSMMMEDDMLQMMMMMAMMMLGMMVFNMLHMN-SKPMMISMNGMLSTS
hADAMTS-5  (AF142099)  (378)  TLGMADVGTMMMSMERSMMVIEDDMMTMAMMTVMMMMMMGMMSMMDD-SKFMMEETFGSTEDK
hADAMTS-1  (AF060152)  (352)  TLGMADVGMMMMDMSRSMMSMVIEDMMMLQMAMMTMMMMMMMGMMMMMMQGASMNGVNQDS
hADAMTS-8  (AF060153)  (332)  TLGMADMGTMMMDMMNMSMVIEDMMMLQMAMMHTLMMMLMMMGMMVMMSMMMDMM-SKPMMTMFMMGMGKH
hADAMTS-2  (AJ003125)  (376)  MQMMAPVTGMMMBVRSMMMMMNMMDGFSMMMEVVMMMMGMMVMMEHMGMGGNRMGDEVRLGS--
nADAMTS-SI            (402)  TLMMAMMMGMMMFMDMYRSMMSMSEDSMMSTMMMIAMMMGMMVFNMMPMMD-NKKMKEE-GVKMPQ
Consensus            (421)  TLGMADVGTICDP RSCSVIEDDGLQAAFT AHELGHVLNMPHDDQSK  C  L  G   S
                              481                                              540

hADAMTS-4  (AB014588)  (388)  RHVMARVMAHVDPEEPMMSPMSARFMMTMMDNGMMGMMLDKMMMGA-PLHLMRVTFMM--KDMMD
hADAMTS-5  (AF142099)  (437)  -RMMMSILTSIDASKEMMSKMMSMATMTEFMMDDGHGNMMEDLMRK-QILGMMEELMMG--QTMD
hADAMTS-1  (AF060152)  (411)  -HMMMASMMSNLDHSQFMMPMSMYMLMSMMDNGHGEMMMDMKMON-MIQLMMGDMMG--TSMMD
hADAMTS-8  (AF060153)  (391)  -HVMMAPLFVHLNQTLFMMSPMSAMYMTELMMDGGHGDMMLDAMGA-ALEMTGMMMRMALMMQ
hADAMTS-2  (AJ003125)  (434)  --RMMAPLMMQAAFHRFHMMSRGMSQQEMMSRMMHS--YDMMLMMDDFFAHDWPALPQLMMG--LHMMS
nADAMTS-SI            (460)  -HVMMAMTENFYTNPWMMMSKRKYIMTEFMMDTGMGMMLNEMMSMMRYEMMVQLMMMMG--ILMMN
Consensus            (481)  RHVMAP L   D   PWSPCSA  ITEFLD GHG CLLD P ARP PLP   LPGRM  YD
                              541                                              600
```
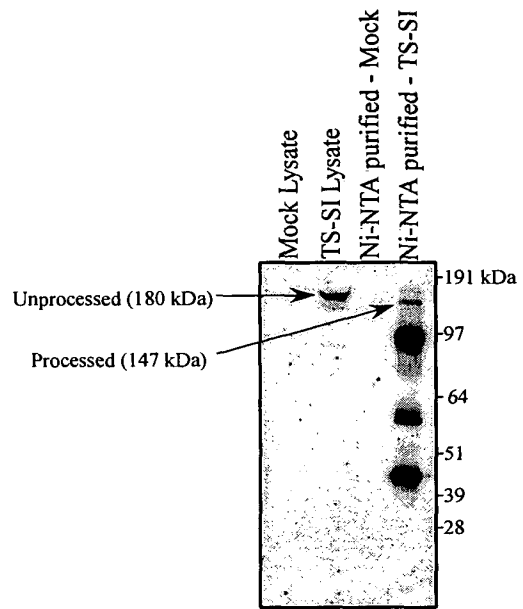
FIG 5

Figure 6

Lane 1 His Ladder (Qiagen)
Lane 2 Empty well
Lane 3 Total lysate
Lane 4 Unbound material
Lane 5 Wash material
Lane 6 50 mM Imidazole Eluate
Lane 7 100 mM Imidazole Eluate
Lane 8 250 mM Imidazole Eluate
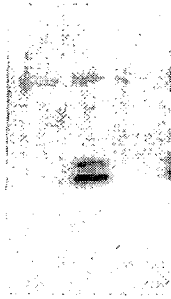Lane 9 2nd 250 mM Imidazole Eluate
Lane 10 Ni-NTA resin

FIG. 7

Mock Lysate
TS-SI Lysate
Ni-NTA purified - Mock
Ni-NTA purified - TS-SI

Unprocessed (180 kDa)
Processed (147 kDa)

191 kDa
97
64
51
39
28

FIG. 8

A   B
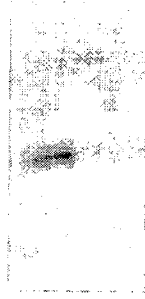
Lane   1   2   3   1   2

Western Blot analysis of ADAMTS-4 and ADAMTS-SI cleavage of aggrecanase substrate. A, lane 1 = uncleaved substrate, lane 2 = ADAMTS-4, lane 3 = ADAMTS-4 + 1 µM compound I.   B, lane 1 = ADAMTS-SI and lane 2 = ADAMTS-SI + 1 µM compound I.